To reflex or not to reflex: genetic testing patterns for neurofibromatosis 1 (NF1) and Legius syndrome

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BACKGROUND

- Germline molecular testing for NF1 and Legius syndrome using next generation sequencing (NGS) and deletion/duplication analysis (del/dup) is being offered by an increasing number of diagnostic laboratories[1]
- Clinicians now have the option to pursue testing for one or both of these genes, concurrently or sequentially, using one or both testing methodologies
- We report data from a single diagnostic laboratory regarding the prevalence of various testing patterns for *NF1* and *SPRED1*, as well as comparative detection rates

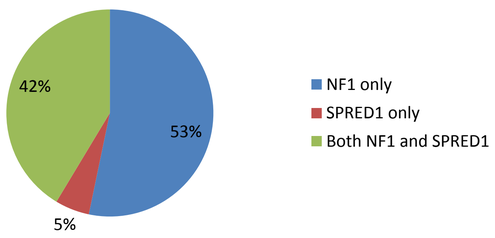
METHODS

- All sequential cases submitted for germline genetic testing of *NF1* and/or *SPRED1* by any testing methodology in any sequence between January 2014 and December 2016 were retrospectively identified
- Cases in which a gene mutation was identified were selected and reviewed

RESULTS

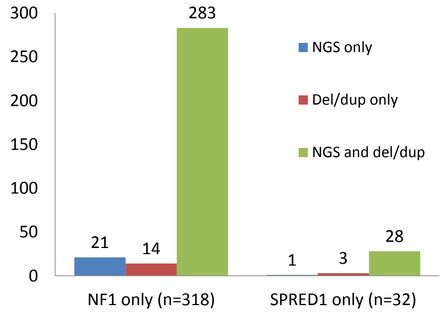
597 probands underwent testing

Gene(s) Tested

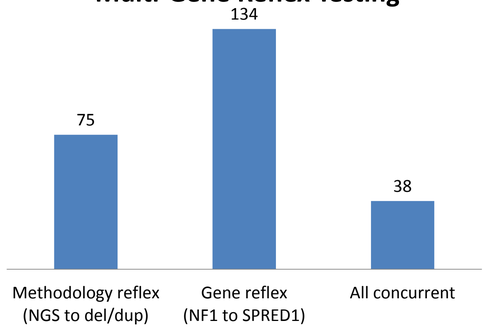


TESTING PATTERNS

Single Gene Testing Methodology



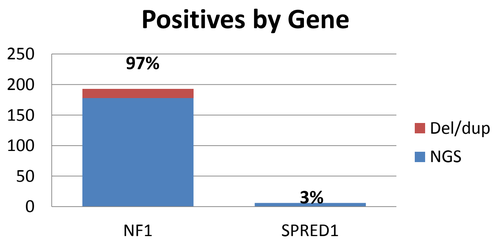
Multi-Gene Reflex Testing



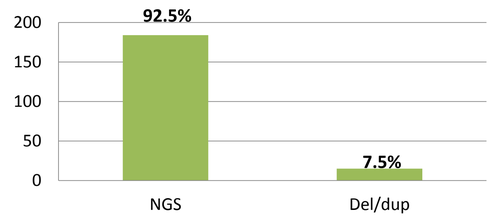
DETECTION RATES

The overall detection rate was 33.3% (199/597)

Positives by Gene



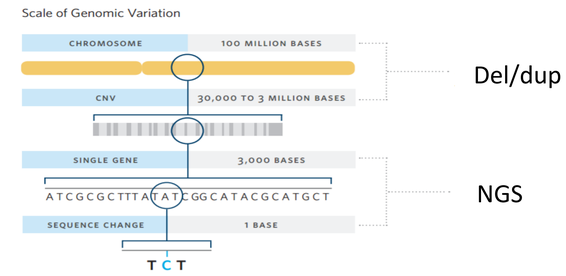
Positives by Methodology



Detection Rate by Test Ordered

	Seq	Del/dup
NF1	32.3% (178/551)	2.9% (15/522)
SPRED1	2.5% (6/238)	0% (0/218)

NGS VERSUS DEL/DUP



TAKE-HOME POINTS

- When ordering molecular testing for *NF1* or *SPRED1*, ***most clinicians (88.9%) order both NGS and del/dup concurrently***
- When testing for both *NF1* and *SPRED1* , ***most clinicians (84.6%) are utilizing reflex testing rather than concurrent testing***
- Although most mutations in this cohort were detected using NGS, ***an important minority of NF1 cases were identified using del/dup***, underlining the need for both methodologies to achieve maximum detection rates for this diagnosis
- Del/dup for *SPRED1* appears less relevant
- There was no significant difference in detection rates for first-round testing if a gene reflex (from *NF1* NGS and del/dup to *SPRED1* NGS) was ordered or if a methodology reflex from (*NF1* and *SPRED1* NGS to *NF1* del/dup) was ordered
- For individuals who have clinical features consistent with both NF1 and Legius, ***there may be no benefit to selecting one type of reflex pattern over the other***; this is particularly relevant when insurance coverage, not clinician preference, dictates the type of testing that can be ordered

REFERENCES

1. https://app.concertgenetics.com/

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